From: "Jon Heuss" <jheuss@airimprovement.com>
To: <ddrechsl@arb.ca.gov>
Cc: "Tom Darlington" <tdarlington@airimprovement.com>; "Cass Andary" <candary@autoalliance.org>
Subject: Comments on Chapter 10
Date: Friday, September 24, 2004 3:23 PM

September 24, 2004

Dr. Deborah Drechsler, Ph. D.
Air Resources Board
Research Division
Sacramento, CA

Dear Dr. Drechsler,

The attached comments on Chapter 10 of the staff's review of the California ozone standard are being submitted to ARB on behalf of the Alliance of Automobile Manufacturers. We appreciate the opportunity to review the material and provide comments. If you have any questions concerning our comments, please do not hesitate to call me at 586-786-0827.

Jon Heuss

Principal Scientist
Air Improvement Resource, Inc.

Comments on Chapter 10 of the June 2004 Public Review Draft "Review of the California Ambient Air Quality Standard for Ozone"

By
Jon M. Heuss
Air Improvement Resource, Inc.

Prepared for the
Alliance of Automobile Manufacturers

September 24, 2004

Introduction

On June 21, 2004 the California Environmental Protection Agency (CalEPA) published a draft report entitled "Review of the California Ambient Air Quality Standard for Ozone." The report was jointly developed by the staff of the Air Resources Board (ARB) and the Office of Environmental Health Hazard Assessment (OEHHA). The report reviews the science of ozone formation, exposure patterns, and ozone health effects and provides staff's recommendations for revisions to the California ozone air quality standard. In particular, the staff recommends retaining the current California 1-hour standard of 0.09 ppm while establishing an 8-hour average standard of 0.070 ppm. Both standards are defined as concentrations "not to be exceeded."

Air Improvement Resource Inc. provided comments on the draft report that were submitted to ARB by the Alliance of Automobile Manufacturers on September 1, 2004.[1] On August 24, 2004, CalEPA made Chapter 10 of the joint report available for public review. Chapter 10 is entitled "Quantifying the Health Benefits of Reducing Ozone Exposures." The stated objective of the chapter is to quantify the adverse health effects of current ozone levels in California by estimating the health benefits that would accrue from a hypothetical control strategy that achieves the proposed ambient air quality standards for ozone. Based on our review, chapter 10 relies on estimated benefits derived from highly uncertain and questionable environmental observational studies that cannot establish causality. As such, chapter 10 overstates the magnitude of the health benefits and the certainty with which they are known. In the following comments we provide detailed evidence supporting this position.

[1] See September 1, 2004 letter from Casimer J. Andary, Director, Regulatory Programs, Alliance of Automobile Manufacturers to Dr. Deborah Drechsler, Air Resources Board and J. M. Heuss and D. F. Kahlbaum, Comments on June 21, 2004 Public Review Draft "Review of the California Ambient Air Quality Standard for Ozone," Air Improvement Resource, Inc. September 1, 2004.

Section 10.1: Health Effects Estimation Approach

The text indicates that staff has drawn considerably from prior efforts at the federal level and specifically refers to the U. S. Environmental Protection Agency (USEPA) Section 812 Report to Congress on the health benefits of federal air pollution regulations. The Section 812 report covers a multitude of regulations and pollutants and is not specifically focused on ozone health benefits. In contrast, the USEPA carried out a health risk analysis specific to ozone in 1996 that is not referenced or considered in chapter 10. This is an extremely important omission.

During the 1996/1997 review of the federal ozone standard, USEPA staff undertook an extensive exposure and risk analysis with input from CASAC. To estimate the risk USEPA used the output of a probabilistic exposure model together with concentration-response functions derived from the clinical studies. The analysis, which is documented in the USEPA Staff Paper, was very conservative as it assumed lung function decrements started at 0.04 ppm, assumed no attenuation of effects, assumed that that children experienced the same level of symptoms as adults (available data suggests otherwise), ignored smoking status that would attenuate responses in outdoor workers, and used human time/activity and exertion data from California as well as other locations. The USEPA analysis also used an algorithm to assign ventilation rates based on individuals who exercised regularly and were motivated to reach a high ventilation rate. As a result, the Staff Paper acknowledged[2] that the analysis allows more high ventilation rates than would actually occur in the populations of interest - outdoor workers, outdoor children, etc.

ARB should either carry out its own exposure analysis (together with concentration-response functions derived from the clinical studies) or use the 1996/1997 EPA analysis to evaluate the number of incidences of lung function decrements and symptoms in order to estimate the benefits of the proposed standards. Such a detailed exposure analysis has an important added benefit in that the whole distribution of personal human exposures is calculated. Since the majority of people spend the majority of their time indoors an understanding of this exposure distribution is critical.

As ARB indicated on page 10-1, estimating health benefits requires estimates of the number of people exposed to ozone and concentration-response functions linking changes in ozone to changes in the incidence of adverse health effects. The clinical studies used to derive the proposed standards are controlled studies thus, when consistent results are obtained, it is clear that ozone is causing the effects. In contrast, environmental observational studies cannot provide causal relationships. Therefore, clinical studies are the more appropriate basis for the concentration-response function. Further, to estimate the risk from the controlled ozone studies, the results must be mapped onto human

[2] See U. S. Environmental Protection Agency, Review of National Ambient Air Quality Standard for Ozone: Assessment of Scientific and Technical Information, OAQPS Staff Paper, EPA-452/R-96-007, June 1996 at page 102.

activity patterns. As ARB indicates, the clinical studies of ozone exposure are the best available data upon which to base a standard. However, the 8-hour exposure protocols are unrealistic so the results must be mapped onto realistic exposure scenarios to determine the actual risk from various alternative standards. The chance of experiencing an exposure of concern requires that the subject be outside at the location of the high ozone and at the time of peak ozone. In addition, in order to experience an exposure that might lead to symptoms or other effects, the subject must be exercising either heavily for approximately one hour or moderately for several hours or more. There are a number of existing ozone exposure studies accounting for the probability of outside exercise at the time and place of peak ozone. The probabilistic exposure modeling carried out by USEPA in its 1996/1997 review is one such study.[3]

Section 10.2: Exposure Estimation and Assumptions

The probabilistic exposure modeling discussed above should be used to develop estimates of the benefits from alternative proposed standards using the results of the clinical studies as the C-R functions.

The text in this section of chapter 10 indicates that there are two key elements -- assessing changes in ozone concentrations and estimating the population exposed to these changes. The change in ozone is calculated assuming a proportional linear rollback of concentrations above a 0.04 ppm background. A significant portion of the chapter is devoted to the analysis of trends at different monitoring sites in the South Coast Air Basin to defend this assumption. However, it is known that ozone formation chemistry is highly non-linear so a linear rollback assumption may not be appropriate. The trends in other California locations should be evaluated to test the assumption.

The estimate of the population exposed to the concentration changes is made by assuming that the population of a county is equally distributed around each monitoring site. This is also a questionable simplification. A more appropriate analysis would be to use population data by census tract and GIS methods to allocate the population to the various monitors.

It is important to note that the population surrounding a monitor is not actually continuously exposed to the concentrations at the monitor. The analysis of exposure in Chapter 7 referenced in Chapter 10, is an analysis of potential peak exposures. The text in Section 7.4 indicates that the tables present information on the population that could be exposed to different peak ozone concentrations. However, since the population spends the majority of its time indoors, and this reduces their exposure, the actual exposure of the population and consequent risk will be below that associated with the reported ambient concentration. This population characteristic must be considered when interpreting the observational studies.

---

[3] U. S. Environmental Protection Agency, Review of National Ambient Air Quality Standard for Ozone: Assessment of Scientific and Technical Information, OAQPS Staff Paper, EPA-452/R-96-007, June 1996.

Section 10.4: Concentration-Response Functions

Since only observational studies are used, the text indicates that subjective judgements are necessary in selecting C-R functions from a wide range available in the literature. As indicated in the September 1, 2004 AIR comments, there are major issues of model selection and potential biases involved in interpreting the air pollution epidemiologic literature. The current practice of using central station monitoring data, central station weather data, and available health statistics yields many weak positive associations for various pollutants in time-series analyses. However, it is known that the methodology is subject to problems of measurement error and exposure misclassification as well as severe collinearity between weather and pollution variables. When the uncertainty due to model selection issues is added and the potential biases noted in the September 1, 2004 AIR comments are considered, the interpretation of a subset of positive findings as causal becomes problematic. Therefore, the use of epidemiological studies for health effect benefit estimation is highly uncertain and the use of controlled studies would be more robust, as employed by EPA in its 1996 ozone review. Nevertheless, we provide the following analysis of ARB's selection of coefficients for various health endpoints.

Section 10.4.4 Mortality from Short-Term Exposure

The text indicates that staff relied on the meta-analysis of Anderson et al. 2004 with support from the Levy et al. 2001 study in developing the C-R function. For the lower limit, they chose the combined result from the revised NMMAPS analysis. There are a number of major problems with this approach. First, the Anderson et al. study reported no association of respiratory mortality with ozone in the meta-analysis of European studies. There were no statistically significant associations of ozone with respiratory mortality in the 12 studies evaluated. The overall risk was 1.000 per 10 $\mu g/m^3$ increase in ozone. Instead, there was a weak signal of an association of ozone with cardiovascular mortality. The finding of a cardiovascular but not respiratory mortality signal from ozone in single pollutant models is hard to explain as a causal relation. It is not coherent with the staff conclusion that the ozone signal in hospital admissions is with respiratory not cardiovascular admissions. In the Anderson study, the combined association of ozone with respiratory hospital admissions was not statistically significant for the five cities available for analysis.

Second, the Anderson et al. analysis evaluated the potential for publication bias and corrected its all-cause ozone/mortality association from 1.003 to 1.002 (95 % CI = 1.000-1.003) using the trim and fill technique. Thus, the staff estimate at a minimum should include a lower effect estimate of zero premature mortality. Anderson et al. discuss the issue of publication bias acknowledging that it is a common and possibly universal problem in our research culture. Furthermore, they note that there are particular reasons why it might occur in time series studies. These include the large number of associations evaluated and the possibility for a selection bias involving the results included in a paper. They also mention a lag selection bias that can be overcome with multi-city studies such as NMMAPS. They further point out that publication bias can result in false conclusions being drawn in the hazard identification stage of a risk assessment and result in an

inflation of the magnitude of the health impacts. They also recognize that the methods of detecting publication bias are not without problems.

Third, the staff uses the Levy et al. estimate to support the choice of the Anderson et al. result but does not mention the strong caveats presented in the Levy et al. paper. Levy et al. describe their result as providing weak epidemiologic support for ozone mortality and as potentially biased because it excludes studies that found ozone to be insignificant. After listing a number of such studies and noting that nearly all the studies found ozone not to be a predictor of mortality including all studies in warmer climates, Levy et al. concludes this information must "…give one pause in using our pooled estimate as a representative measure of ozone mortality risks." They also discuss the difficulties of separating temperature or weather and ozone effects, cautioning that "possible confounding by weather leaves lingering doubt about whether the ozone findings are causal, an issue that would be difficult to resolve epidemiologically."

Fourth, the staff improperly uses the combined result from lag 0 single pollutant ozone models in the NMMAPS re-analysis for the lower bound estimate. The NMMAPS re-analysis reported a positive association for ozone with mortality in the summer but a negative association in the winter at lag 0. The lag 0 results were stronger than the lag 1 and lag 2 results. However, an association of ozone at lag 0 may be problematic since the ozone peaks in the afternoon and mortality is distributed throughout the day so that a lag 0 association potentially runs afoul of the temporality requirement that the cause precede the effect.

In closing, the lower estimate should be zero based on the following factors: the wide range of individual city results in NMMAPS and other meta-analyses, the overall negative winter association demonstrated in NMMAPS, the lack of a significant summer combined association for the 90 largest U. S. cities in NMMAPS multi-pollutant models, and the several other concerns that leave doubt about causality. The only reported NMMAPS ozone results in multi-pollutant models were for the summer. In each case, when other pollutants were included, the ozone association was reduced and became non-significant. If the ozone associations are not robust to inclusion of other pollutants in the summer when there was a combined positive association in single pollutant models, it is very unlikely that they could be causal. In the September 1, 2004 AIR comments, we provided staff with the individual city summer ozone results demonstrating a very wide range of associations, both positive and negative in single pollutant models.

Section 10.4.5: Hospital Admissions for Respiratory Disease

Chapter 10's estimate for the association of ozone with all respiratory hospital admissions comes from Thurston and Ito, 1999. Levy et al. 2001 relied on the same meta-analysis, but cautioned that the estimate is based exclusively on studies in cold climates. They also note that two Medicare-based studies listed by Thurston and Ito occurred in a warmer climate (Birmingham, Alabama) and neither found a statistically significant relationship. Levy et al. also noted that ozone has not shown a consistent association with

cardiovascular hospital admissions, consequently this outcome was not included in their estimate of ozone health benefits.

There is no use of California-based hospital admission studies in this section despite references in this section and in the Section 10.1 introductory paragraph stating that hospital admissions studies were conducted in California and were included in the analysis wherever possible. Because of the relevance of California studies to setting California air quality standards, the available California studies should be used in the benefits analysis. Such studies exist, and many of the results, as acknowledged in Chapter 12, indicate negative findings. Instead of using California studies, this section of chapter 10 relies heavily on several multi-city Canadian and eastern U. S. studies. However, as shown in the NMMAPS analyses, the range of individual city results in multi-city analyses with a consistent methodology is very large and not biologically plausible. Combining results that are not biologically plausible may provide an overall association that likely represents residual confounding. The wide range also indicates that individual city studies are not reliable.

Given the many issues acknowledged in Section 12.2.1 as well as issues raised in the September 1, 2004 AIR comments, the only conclusion that can be drawn is that despite many positive ozone associations with hospital admissions in the literature, individual city studies are not reliable due to model selection issues; multi-city studies are suspect, too. This conclusion is consistent with the emerging realization in the scientific community that there is increasing evidence for caution in interpreting weak air pollution associations. In order to fully consider the range of ozone/hospital admissions associations in the literature, the presence of negative studies must be acknowledged and the lower limit should be zero.

Section 10.4.7: School Absences

The Gilliland et al. 2001 study of school absences is important but it is the only study of its type. As noted in several places in Chapter 12, there is a question of residual seasonal confounding for this study. Furthermore, a substantially larger effect in low ozone communities versus the effect in high ozone communities, a highly counterintuitive result, necessitates additional explanation. . Potential confounding by bioaerosols was not evaluated in the study. Thus, it would be particularly important to replicate the study in another cohort and over all seasons. The many issues with model selection that have arisen in recent years raise additional concerns that the result may not be robust.

The large reported ozone effect on respiratory absences seems disproportional to the lack of substantial effects on respiratory symptoms seen in school children residing in the Basin. Chapter 12 acknowledges that there are several studies of respiratory symptoms in California that failed to detect symptomatic effects. These include Delfino et al. 1996, Delfino et al. 1997b, Linn et al. 1996, and Ostro et al. 2001. There is a particularly important study of asthmatic, wheezy, and healthy children in Southern California that is

not mentioned in Chapter 12. The Health Effects Institute study by Avol et al.[4] evaluated potential acute respiratory effects of ambient ozone in the spring and the summer. About 200 10 to 12 year old children from Lancaster, San Dimas, Upland, Mira Loma, Riverside and Lake Arrowhead were studied in the spring and late summer of 1994 with monitored hourly ozone levels exceeding the federal 1-hour standard in each season and with peak hourly levels up to 200 ppb in the summer period.

There was no consistent or clear role of ozone in producing changes in reported symptoms or medication use. There was also no discernible pattern of diurnal lung function changes by season, by ozone level, or by health group. The authors note that failure to detect clear evidence of acute pulmonary effects in the three groups may be due to insufficient elevation of ozone levels during the study, although ozone concentrations exceeded 80 ppb during the study. The authors note that children in their study on average did not spend a comparable amount of time outdoors or exercising at the high levels to the time used in the chamber studies.

The lack of a substantial respiratory symptom signal in several California studies is inconsistent with the large effect on school absences reported by Gilliland. This difference needs to be acknowledged and discussed in the chapter.

Section 10.4.8: Minor Restricted Activity Days

The authors use an association of two-week average ozone with minor restricted activity days from Ostro and Rothschild, 1989 for this endpoint. They note that the association with ozone was highly variable but statistically significant. They also note that there was no association with respiratory-related restricted activity days (RRAD). Minor Restricted Activity Days (MRADs) are days when people reduce their activity but do not miss work or school.

Levy et al. 2001 point out some statistical issues with the study. They raise concerns that the study may not properly measure an independent ozone effect. They note that of the six years in the study, 1976-1981, the regression coefficient was significantly negative in 1977 and 1981. Although the combined result was significantly positive, Levy et al. caution that the magnitude of the ozone impact on MRAD should be considered somewhat uncertain given that “only one older study with statistical issues is available.”

Since ozone was not significantly associated for any year with RRAD, it is difficult to discern what the actual health effect on a MRAD might be and how it could be caused by ozone. Given these issues and the presence of negative as well as positive study results, the lower bound estimate should be zero.

[4] E. Avol, et al., Acute effects of ambient ozone on asthmatics, wheezy, and healthy children, Health Effects Institute Report Number 82, 1998.

Presentation and Discussion of Health Effects Results

As explained in Section 10.6, as well as in these comments, there are additional uncertainties not reflected in the Tables in Section 10.5. The most important uncertainty relates to the assumption of causality. The text in Section 10.6 alludes to this uncertainty by referring to a lack of sensitivity analyses "…that would be most useful in judging whether ozone is an independent risk factor for acute mortality." As indicated above there are valid reasons for assuming that the lower limit for the various observational study endpoints evaluated in the Chapter is no effect. .

The second most important uncertainty is due to the assumption of no threshold for most of the evaluated endpoints. Section 10.6 acknowledges that about 76 to 86 % of the estimated benefits accrue at concentrations between the proposed standards and the background. The discussion in Chapter 10 indicates only a few ozone studies have examined the shape of the concentration-response function. The Special Panel of the HEI Review Committee recently raised several cautions in interpreting epidemiological concentration-response results. They point out[5] that measurement error could obscure any threshold that might exist and note that city-specific concentration-response curves for particulate matter exhibited a variety of shapes. They also caution that the standard approach of minimizing the Akaike Information Criterion may not be appropriate for choosing between models. The HEI Panel finally cautions that lack of evidence against a linear model should not be confused with evidence in favor of it. The use of a linear ozone effect model as the default should not be accepted until it is demonstrated with controlled studies that low doses within the range of background are capable of eliciting significant biological effects. In addition, a sensitivity analysis to alternative formulations of the C-R function should be carried out.

[5] See Commentary in HEI Research Report Number 94, Part III, May 2004.